



Pre-Exposure Prophylaxis (PrEP): A Rising Star in HIV Prevention Research?

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BACKGROUND

COULD A PILL A DAY KEEP HIV AWAY?

An array of antiretrovirals are used to treat acquired HIV infection. Some antiretrovirals are also used to prevent it shortly after blood-borne or sexual exposure (post-exposure prophylaxis) or perinatally (mother-to-child transmission). Several animal studies suggest that antiretrovirals taken before exposure may provide protection. With slow progress—and recent setbacks—in HIV non behavioral prevention research (vaccine, microbicides...), HIV PrEP might become the next available tool in the limited biomedical weaponry for HIV prevention.

OBJECTIVES

- This study aimed to:
- identify all past, current, and planned HIV oral antiretroviral PrEP clinical trials;
 - synthesize descriptive characteristics of HIV oral antiretroviral PrEP clinical trials.

METHODS

SYSTEMATIC REVIEW

A systematic search of HIV oral antiretroviral PrEP prospective controlled studies was conducted. Information sources included trial registries (NIH, MetaRegister, WHO's ICTRP, Cochrane's Central), electronic databases (Medline, Embase), specialized websites (PrEP Watch, MTN, HPTN), the internet (Google engine), and involved investigators and sponsors. Targeted source documents were trial registry files, study protocols, study reports, and related information made publicly available by involved investigators and sponsors. Neither animal studies nor topical antiretrovirals were included. Pre-defined data items were extracted and synthesized.

RESULTS

STATUS & FOCUS OF HIV ORAL PrEP TRIALS

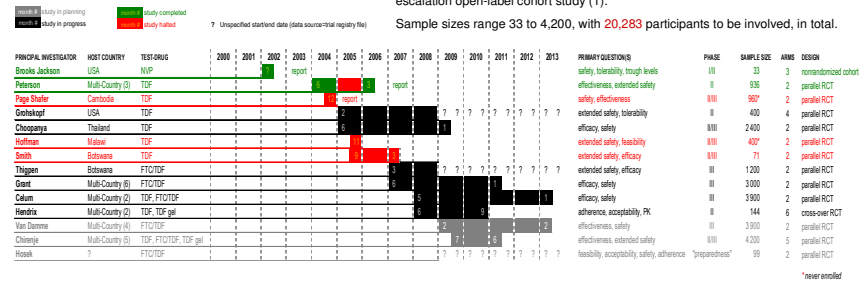
14 trials were identified: 2 completed and published, 3 prematurely stopped, 6 ongoing, and 3 in planning, all within current decade. Studies' primary questions include feasibility (2), safety (13), efficacy/effectiveness (9), and adherence (2).

DESIGN & SIZE OF HIV ORAL PrEP TRIALS

One trial is described as a pilot, one as phase I/II, three as phase II, five as phase II/III, and four as phase III. Trials feature 2 to 6 arms and 3 types of designs: parallel blinded randomized trials (12), randomized open-label cross-over trial (1), and non-randomized dose-escalation open-label cohort study (1). Sample sizes range 33 to 4,200, with 20,283 participants to be involved, in total.

HIV ORAL PrEP TRIALS' SPONSORS

All 14 studies (100%) have one or more of their primary sponsors based in the United States of America. Those US sponsors include 3 governmental organizations (Centre for Disease Control and prevention, National Institutes of Health, US Agency for International Development), 2 non governmental organizations (Bill and Melinda Gates Foundation, Family Health International), 1 academic institution (University of Washington) and 1 pharmaceutical company (Gilead Sciences, Inc.).



CONCLUSION

Early HIV PrEP studies have been associated with public controversies due to ethical concerns in host communities, which led to forced closure of some trials. The approach now seems to generate more positive interest and more support. This is after multiple rounds of international consultations were conducted, and bioethics recommendations for HIV biomedical prevention trials were developed. It would be important to assess how these guidelines (UNAIDS 2007, Institute of Medicine 2008) might have influenced scientists involved in HIV PrEP research and what impact they may have on the progress of this novel field.

COUNTRIES HOSTING HIV ORAL PrEP TRIALS

17 countries worldwide have been considered for hosting HIV oral PrEP trials. 6 of the 14 trials are multinational, each involving 2 to 6 countries across 3 continents. 9 studies were set to be hosted in Africa, 5 in Northern America, 3 in South-Eastern Asia, and 1 in Latin America.



INTERVENTIONS & CO-INTERVENTIONS IN HIV ORAL PrEP TRIALS

Three oral antiretrovirals have been considered: nevirapine (NVP) in 1 trial, tenofovir (TDF) in 9 trials, and emtricitabine/tenofovir (FTC/TDF) in 6 trials. Three trials include head-to-head evaluation of tenofovir pills and/or emtricitabine/tenofovir pills and/or topical tenofovir. Co-interventions include provision of risk-reduction counseling, male and/or female condoms, contraceptive products, treatment for sexually transmitted infections, and hepatitis B vaccination.



POPULATIONS STUDIED IN HIV ORAL PrEP TRIALS

Studies target heterosexual men (4), heterosexual women (8), men having sex with men (4), injection drug users (2), and serodiscordant couples (1); 3 studies have mixed populations. All participants were/are to be healthy and over 18 years of age -or- legally able to consent, at screening.



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